REMARKS

Claims 1-26 are pending. Claim 23 is currently amended. No new matter has been introduced by virtue of the amendment made herein. Accordingly, Applicants respectfully request entry of the amendment made herein.

In view of the amendment made herein and the remarks below, Applicants respectfully request reconsideration and withdrawal of the rejections set forth in the September 14, 2006 Office Action.

Rejection Under 35 USC § 112, ¶ 2

Claims 1-3, 22, and 23 have been rejected under 35 U.S.C. § 112, ¶ 2 for allegedly being indefinite. In particular, Claims 1-3 and 23, which recite a starch having a particular tensile strength, stand rejected because the term "tensile strength" is allegedly indefinite. According to the Office Action, the claims fail to disclose "[the] physical form [of the starch] (free powder or compressed with other ingredients) or how the tensile strength was measured." Applicants respectfully submit that the claims are not indefinite for the reasons that follow.

The claims of the present application are directed to a sustained-release pharmaceutical composition of pramipexole, dispersed in a matrix comprising a hydrophilic polymer and a starch having a minimum tensile strength requirement "at a solid fraction representative of the tablet." Applicants respectfully submit that the claim phrase "at a solid fraction representative of the tablet" addresses the issues raised in the Office Action. In particular, the term "solid fraction" is specifically defined in the present application as "the ratio of absolute to apparent density of a *starch* compact." *See* App. at p. 4, ¶ [0019] (emphasis added). A "compact" is defined as a "compressed tablet," "consisting *only* of a sample of *starch*." *See id.* (emphasis added). Finally, the present application discloses that the tensile strength determination is based on the *starch compact* as defined above. *See, e.g.,*

claimed feature does not render the claims indefinite – where all of the conventional methods used to measure the claimed feature produce essentially the same results. *See PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1563 (Fed. Cir. 1996). In the present context, the specification of the present application clearly provides that "[t]ensile strength of a starch sample can be measured by any suitable test." *See id.* at ¶ [0046]. The application then goes on to provide several different examples of tests that can be used – e.g., "triaxial test"; "4 second dwell time test"; and "90 second dwell time test." *See id.* at ¶¶ [0046] [0061]. The tensile strength of six different lots of starch samples were each tested three times – using the triaxial, 4 second dwell time, and 90 second dwell time tests. The results, which are provided in Tables 1 and 2 of the specification, demonstrate that the value for tensile strength of each respective lot was essentially the same under the different tensile strength tests. Accordingly, under *PPG Industries*, the rejection should be withdrawn.

Insofar as the rejection of Claim 22 is concerned, the Office Action alleges that the term "nonfunctional coating" is not adequately defined within the claim. Applicants respectfully request reconsideration and withdrawal of that rejection. As the Office Action recognizes, the term is "adequately defined" in the specification. *See* Office Action at p. 2. The specification explicitly provides that the "nonfunctional coating" is an additional coating of the pharmaceutical composition that has "no substantial effect on the release properties of the tablet." *See* App. at ¶ [0076]. Accordingly, the term "nonfunctional coating" simply means any coating that can be used on a pharmaceutical dosage form, other than one that controls the release characteristics of the active ingredient.

Insofar as the rejection of Claim 23 is concerned, Applicants have amended the claim to remove the objected to language concerning the alleged trademark/trade name "HPMC type 2208." Accordingly, it is respectfully submitted that the above rejection has been overcome.

Rejection Under 35 USC § 102

hydrophilic polymer and a starch having a particular, minimum tensile strength requirement. In contrast, Holman discloses the use of MIRAPEX® — an *immediate release*, pramipexole dosage form that needs to be administered three-times-a-day to patients suffering from CNS disorders. An immediate-release pramipexole dosage form cannot anticipate a sustained-release pramipexole composition. Thus, the rejection should be withdrawn.

In addition, Holman fails to disclose the inclusion of a starch having a tensile strength of at least about 0.15 kN cm^{-2} in such composition. To overcome this deficiency in Holman, the Office Action alleges that Holman's disclosure of a pregelatinized starch – without any reference to its tensile strength – is sufficient to establish anticipation because "the same compound [i.e., the starch] will have the same properties, such as tensile strength, when compressed under the same amount of force to form a tablet form." *See* Office Action at p. 4. Applicants respectfully submit that the above allegation is incorrect, and, in fact, contradicted by the disclosure of the present application. In particular, the specification of the present application confirms that the values of tensile strength, as determined for six different lots of *pregelatinized starch,* can, and in fact, do vary from lot to lot. *See* App. at Table 1. Indeed, Paragraph [0088] of the present application provides: "A great variation in tensile strength of pregelatinized starches was observed." Moreover, as shown in Table 1, and as further explained in Paragraph [0088], even different lots that were obtained from the *same* manufacturer were shown to have different tensile strengths: (1) lots 3 and 4, which were from the same manufacturer, showed values of 0.074 and 0.119, respectively; and (2) lots 1, 5, and 6, from a second manufacturer, showed values of 0.323, 0.287, and 0.236, respectively. Accordingly, there is no basis to support the statement in the Office Action that the pregelatinized starch used Holman has the same tensile strength as claimed in the present invention because it would have been compressed into a tablet. Rather, the evidence demonstrates that different starches, and indeed, different lots of the same starches, can have differing tensile strengths. Consequently, Applicants respectfully submit that the 102(e) rejection based on Holman should be withdrawn.

tensile strength, when compressed under the same amount of force to form a tablet form." *See* Office Action at p. 5. For the reasons that follow, the rejection should be withdrawn.

First, Patel allegedly provides solid pharmaceutical compositions for improved delivery of a "wide variety of pharmaceutical active ingredients." *See* Patel at ¶ [0045]. In this regard, Patel merely provides a "laundry list" – which, in fact, goes on for ten (10) pages (*see* Patel at pp. 3-13) of active ingredients that may be contemplated, in which pramipexole is buried. Similarly, Patel provides a "laundry list" of excipients that can be incorporated into such compositions; and Patel contemplates various types of dosage forms – i.e., such as delayed release, immediate release, targeted delayed release, fast-disintegrating coatings, etc. *But* there is no specific teaching in Patel of a sustained-release pramipexole composition, dispersed in a matrix comprising a hydrophilic polymer and a starch – much less a starch having a particular tensile strength. Moreover, as demonstrated above in respect to the Holman rejection, Patel's disclosure, in general, of a pregelatinized starch is not an inherent disclosure of the claimed tensile strength limitation of the starches used in the presently claimed invention. Consequently, because Patel fails to disclose the use of a starch having a tensile strength of at least 0.15 kN cm^{-2}, Applicants respectfully submit that the 102(e) rejection based on Patel should be withdrawn.

Rejection Under 35 USC § 103(a) Of Claims

Claims 1-22 and 24-26 have further been rejected as allegedly being obvious under 35 U.S.C. §103(a) in view of Holman (alone). Similarly, Claims 1-26 have been rejected as allegedly being obvious under 35 U.S.C. §103(a) in view of Patel (alone).

In response, Applicants submit that a *prima facie* case of obviousness has not been established and respectfully request reconsideration and withdrawal of the rejections. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Third, the prior art reference (as

motivation. Accordingly, Applicants respectfully submit that the rejections should be withdrawn.

Finally, Claims 1-26 have been rejected as allegedly being obvious under 35 U.S.C. §103(a) in view of Holman in view of Khan (U.S. Pat. No. 5,656,296) and Petrus (WO 00/59477) and in further view of Michaud (EP 0933079).

In response, the Applicants submit that the combination of Khan, Petrus and Michaud with Holman does not cure the deficiency of Holman as set forth above – i.e., that Holman (and Patel, for that matter) fail to teach or suggest sustained-release pramipexole compositions containing a starch having a tensile strength of about 0.15 kN cm^{-2}. In this regard, as set forth in the Office Action, neither Khan nor Petrus were even cited for the purpose of establishing the starch-tensile strength limitation of the present invention. Rather, the Office Action relies solely on Michaud in an effort to establish that "pregelatinized starch was already known to have tensile strength within applicants' claimed amounts when compressed into a tablet form." *See* Office Action at p. 8. In response, the Applicants submit that the rejection should be withdrawn for the reasons that follow.

First, Michaud is directed to tablets that are capable of *rapid disintegration* in an aqueous medium – which is in direct contrast to the *sustained-release* compositions of the present invention. Second, Michaud does not, in fact, disclose the use of a starch having a tensile strength of at least 0.15 kN cm^{-2}. Rather, Michaud describes *tablets* (comprising other ingredients *in addition to* the starch) that have a particular tensile strength. Thus, the final tablet – not the starch alone – is described as having a particular tensile strength. Accordingly, Applicants respectfully submit that there is no reasonable expectation of success in applying the teaching of Michaud and Holman to arrive at the instant application.

In this regard, Applicants submit that one having ordinary skill in the art would not apply the *rapidly-disintegrating* tablets of Michaud with the *immediate-release* MIRAPEX® composition of Holman to arrive at the *sustained-release* compositions of the present invention. Indeed, even if, assuming for the sake of argument only, one were to combine the references, the combination of two immediate-release technologies would not produce a sustained-release composition. Moreover, such a combination would additionally fail to

Conclusion

In view of the remarks above and the amendments submitted herein, Applicants respectfully submit that the pending claims are fully allowable, and solicit the issuance of a notice to such effect. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact applicants' undersigned attorneys at the telephone number provided.

The Commissioner is hereby authorized to charge any fees required or to credit any overpayment to Deposit Account No. 16-1445.

Respectfully submitted,

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